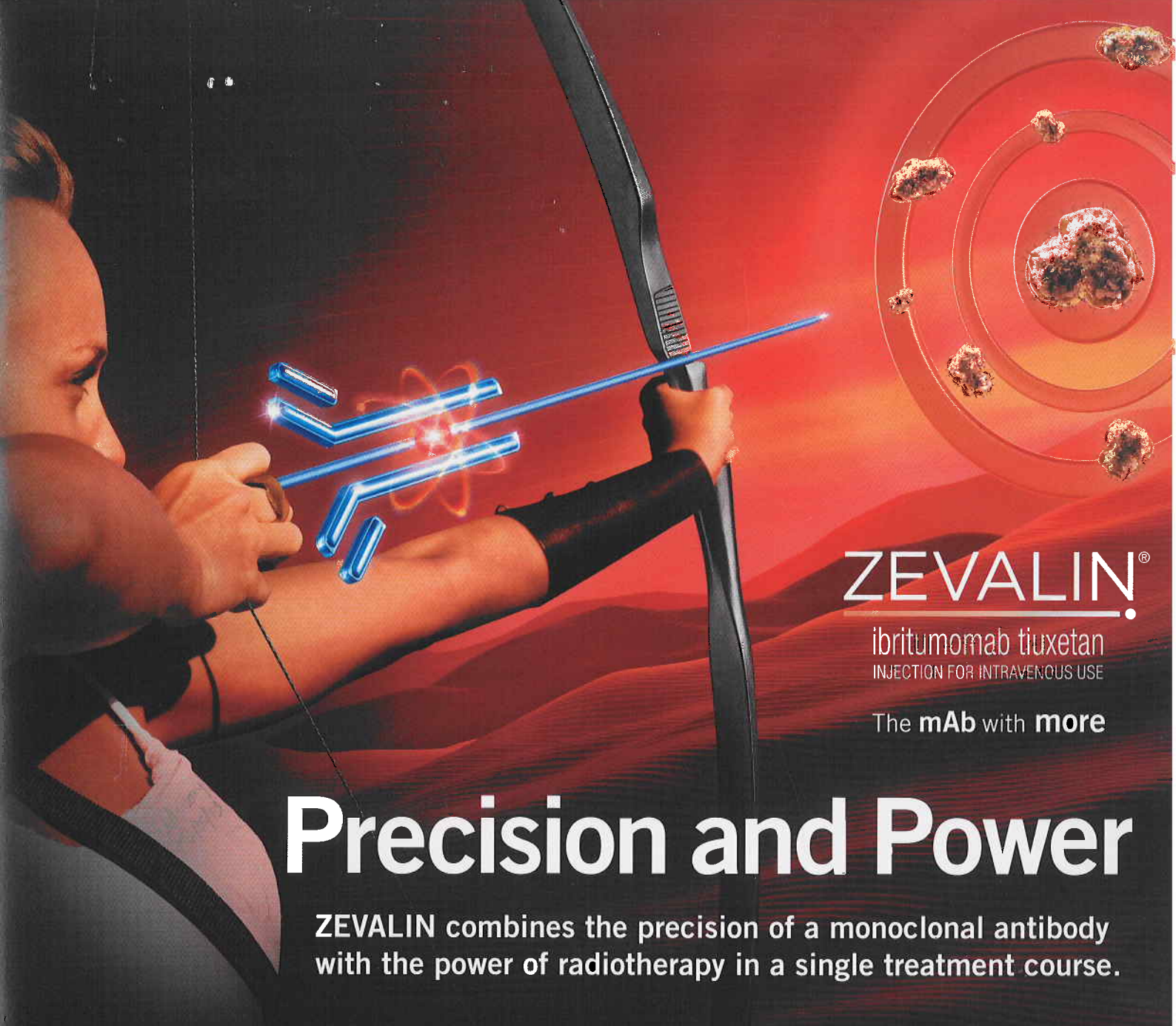


ZEVALIN®

ibritumomab tiuxetan

INJECTION FOR INTRAVENOUS USE

The **mAb** with **more**

Precision and Power

ZEVALIN combines the precision of a monoclonal antibody with the power of radiotherapy in a single treatment course.

Indications and Usage

ZEVALIN® (ibritumomab tiuxetan) is a CD20-directed radiotherapeutic antibody administered as part of the ZEVALIN therapeutic regimen indicated for the treatment of patients with:

- Relapsed or refractory, low-grade or follicular B-cell non-Hodgkin's lymphoma (NHL)
- Previously untreated follicular NHL who achieve a partial or complete response to first-line chemotherapy

Important Safety Information

WARNING: SERIOUS INFUSION REACTIONS, PROLONGED AND SEVERE CYTOPENIAS, and SEVERE CUTANEOUS AND MUCOCUTANEOUS REACTIONS

See full Prescribing Information for complete boxed warning.

- Serious Infusion Reactions, some fatal, may occur within 24 hours of rituximab infusion.
- Prolonged and Severe Cytopenias occur in most patients.
- Severe Cutaneous and Mucocutaneous Reactions, some fatal, reported with ZEVALIN therapeutic regimen.
- Do not exceed 32 mCi (1184 MBq) of Y-90 ZEVALIN.

Please see Important Safety Information on inside front cover. Please see full Prescribing Information, including BOXED WARNINGS, for ZEVALIN included in the back pocket. Because the ZEVALIN therapeutic regimen includes the use of rituximab, please also consult Prescribing Information for rituximab (www.rituxan.com).

Indications and Usage

ZEVALIN® (ibritumomab tiuxetan) is a CD20-directed radiotherapeutic antibody administered as part of the ZEVALIN therapeutic regimen indicated for the treatment of patients with:

- Relapsed or refractory, low-grade or follicular B-cell non-Hodgkin's lymphoma (NHL)
- Previously untreated follicular NHL who achieve a partial or complete response to first-line chemotherapy

Important Safety Information

WARNING: SERIOUS INFUSION REACTIONS, PROLONGED AND SEVERE CYTOPENIAS, and SEVERE CUTANEOUS AND MUCOCUTANEOUS REACTIONS

Serious Infusion Reactions: Deaths have occurred within 24 hours of rituximab infusion, an essential component of the ZEVALIN therapeutic regimen. These fatalities were associated with hypoxia, pulmonary infiltrates, acute respiratory distress syndrome, myocardial infarction, ventricular fibrillation, or cardiogenic shock. Most (80%) fatalities occurred with the first rituximab infusion. Discontinue rituximab and Y-90 ZEVALIN infusions in patients who develop severe infusion reactions.

Prolonged and Severe Cytopenias: Y-90 ZEVALIN administration results in severe and prolonged cytopenias in most patients. Do not administer Y-90 ZEVALIN to patients with ≥25% lymphoma marrow involvement and/or impaired bone marrow reserve.

Severe Cutaneous and Mucocutaneous Reactions: Severe cutaneous and mucocutaneous reactions, some fatal, can occur with the ZEVALIN therapeutic regimen. Discontinue rituximab and Y-90 ZEVALIN infusions in patients experiencing severe cutaneous or mucocutaneous reactions.

Dosing: The dose of Y-90 ZEVALIN should not exceed 32.0 mCi (1184 MBq).

Leukemia and Myelodysplastic Syndrome: Among 204 patients receiving Y-90 ZEVALIN following first-line chemotherapy, two patients (1%) were diagnosed with AML within 3 years of receiving ZEVALIN.

Myelodysplastic syndrome (MDS) and/or acute myelogenous leukemia (AML) were reported in 5.2% (11/211) of patients with relapsed or refractory NHL enrolled in clinical studies and 1.5% (8/535) of patients included in the expanded-access trial, with median follow-up of 6.5 and 4.4 years, respectively. Among the 19 reported cases, the median time to diagnosis of MDS or AML was 1.9 years following treatment with the ZEVALIN therapeutic regimen; however, the cumulative incidence continues to increase.

Embryo-fetal Toxicity: May cause fetal harm if given during pregnancy.

Extravasation: Monitor for extravasation and terminate infusion if it occurs. Resume infusion in another limb.

Immunization: Do not administer live viral vaccines to patients who recently received ZEVALIN.

Laboratory Monitoring: Obtain complete blood counts (CBC) and platelet counts at least weekly.

Radionuclide Precautions: During and after radiolabeling ZEVALIN with Y-90, minimize radiation exposure to patients and to medical personnel, consistent with institutional good radiation safety practices and patient management procedures.

Additional Important Safety Information

Creutzfeldt-Jakob Disease (CJD): The ZEVALIN therapeutic regimen contains albumin, a derivative of human blood. Based on effective donor screening and product manufacturing processes, ZEVALIN carries an extremely remote risk for transmission of viral diseases. A theoretical risk for transmission of CJD also is considered extremely remote. No cases of transmission of viral diseases or CJD have ever been identified for albumin.

Impairment of Fertility: There is a potential risk that the ZEVALIN therapeutic regimen could cause toxic effects on the male and female gonads. Effective contraceptive methods should be used during treatment and for up to 12 months following the ZEVALIN therapeutic regimen.

Nursing Mothers: Patients should be advised to discontinue nursing during and after ZEVALIN treatment.

Adverse Reactions: The most common adverse reactions of ZEVALIN are cytopenias, fatigue, abdominal pain, nausea, nasopharyngitis, asthenia, diarrhea, cough, and pyrexia. Common adverse reactions (≥40%) in clinical trials were: neutropenia, leukopenia, thrombocytopenia, anemia, infection, asthenia, musculoskeletal symptoms, and gastrointestinal symptoms. The most serious adverse reactions of ZEVALIN are prolonged and severe cytopenias (thrombocytopenia, anemia, lymphopenia, neutropenia) and secondary malignancies.

When administered following first-line chemotherapy, grade 3/4 adverse reactions of ZEVALIN include prolonged and severe cytopenias (thrombocytopenia [51%], neutropenia [41%], leukopenia [36%], lymphopenia [18%], and anemia [5%]) and secondary malignancies. Cytopenias were more severe and more prolonged among eleven (5%) patients who received ZEVALIN after first-line fludarabine or a fludarabine-containing chemotherapy regimen as compared to patients receiving non-fludarabine-containing regimens. Grade 3/4 infections occurred in 8% of ZEVALIN-treated patients and in 2% of controls and included neutropenic sepsis (1%), bronchitis, catheter sepsis, diverticulitis, herpes zoster, influenza, lower respiratory tract infection, sinusitis, and upper respiratory tract infection.

Grade 3/4 adverse reactions of ZEVALIN in relapsed or refractory NHL patients include prolonged and severe cytopenias (thrombocytopenia [63%], neutropenia [60%], anemia [17%], and ecchymosis [<1%]) and secondary malignancies. Serious infections occurred in 3% of patients (urinary tract infection, febrile neutropenia, sepsis, pneumonia, cellulitis, colitis, diarrhea, osteomyelitis, and upper respiratory tract infection). Life-threatening infections were reported in 2% of patients (sepsis, empyema, pneumonia, febrile neutropenia, fever, and biliary stent-associated cholangitis).

Please see full Prescribing Information, including BOXED WARNINGS, for ZEVALIN included in the back pocket. Because the ZEVALIN therapeutic regimen includes the use of rituximab, please also consult Prescribing Information for rituximab (www.rituxan.com).

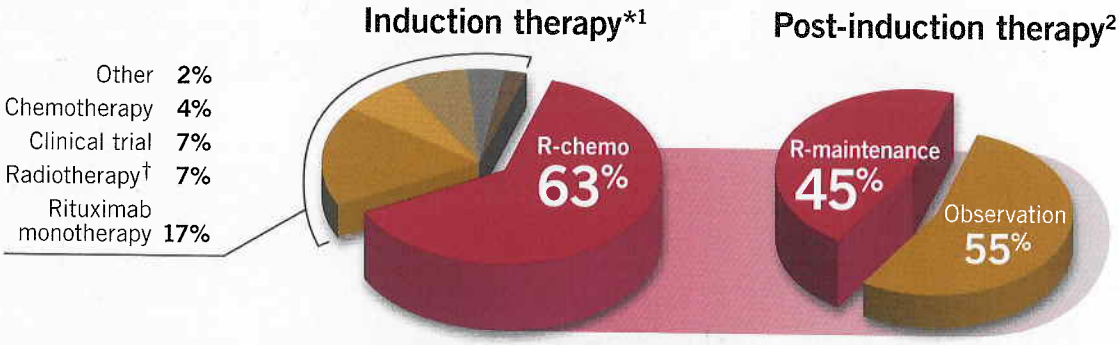
ZEVALIN®
ibritumomab tiuxetan
INJECTION FOR INTRAVENOUS USE

The **mAb** with **more**

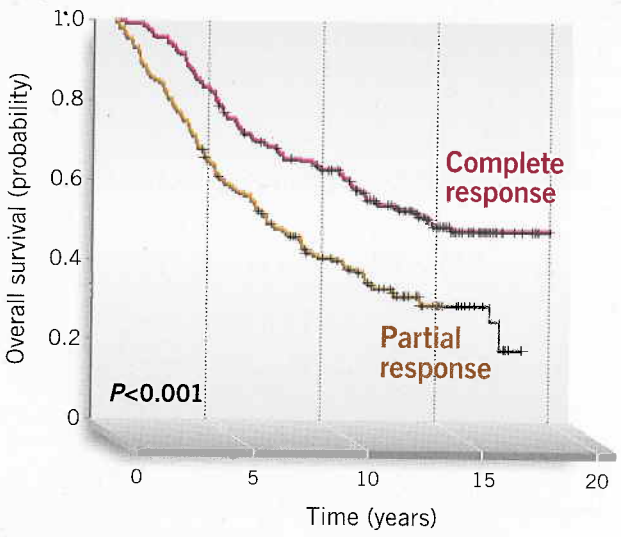
First-line therapy in follicular lymphoma is well-established

Many patients receive rituximab-chemotherapy followed by rituximab-maintenance

The 2004–2007 National LymphoCare study evaluated first-line treatment choices for follicular lymphoma at both induction and post-induction phases.[1,2]



Patients reaching complete response after first-line treatment are more likely to experience improved overall survival[3]



- Patients achieving a complete response had improved long-term survival versus patients who experienced a partial response (PR) at any time during the study period
- Data from this study suggest a strong correlation between response quality after first-line treatment (complete response) and survival

The Groupe d'Etude des Lymphomes de l'Adulte (GELA) enrolled 536 patients from 1986 through 1995 in a long-term prospective analysis designed to assess the correlation between response quality to first-line therapy and overall survival.

* Excluding observation. Percentages are based on data provided in the National LymphoCare study. The choice to observe rather than initiate therapy was associated with age, FLIPI, stage, and grade ($P<0.01$). 18% and 46% of patients were observed in induction and post-induction phases, respectively.

† External beam radiotherapy was employed in this study.

ZEVALIN® (ibritumomab tiuxetan) treatment regimen is NOT indicated for first-line treatment in previously untreated follicular lymphoma patients prior to chemotherapy. There are no FDA-approved clinical data comparing the efficacy of ZEVALIN to R-maintenance.

First-line treatment can fall short

INDUCTION

In many patients, R-chemo and R-monotherapy induction therapies fail to deliver a complete response (CR/CRu)

Study	n	Treatment	Response rates		
			ORR‡	CR/CRu	PR
Ghielmini et al., 2004[4]	57	R-monotherapy	67%	9%	58%
Czuczman et al., 1999[5]	40	R-CHOP	95%	55%	40%
Hiddeman et al., 2005[6]	223	R-CHOP	96%	20%	77%
Marcus et al., 2005[7]	162	R-CVP	81%	41%	40%
Salles et al., 2010[8]	1018	R-CHOP/R-CVP/R-FCM	–	71%	29%
Rummel et al., 2012[9]	261	B-R	93%	40%	53%
	253	R-CHOP	91%	30%	61%

‡ Overall response rate

R-MAINTENANCE (2 years)

And many patients relapse soon after post-induction R-maintenance

The Phase III PRIMA trial compared the efficacy of R-maintenance vs. no further treatment in patients who responded to R-chemotherapy as first-line treatment. Results from this trial show:[8§]

14% Patients failed R-maintenance therapy

POST-MAINTENANCE (1 year)

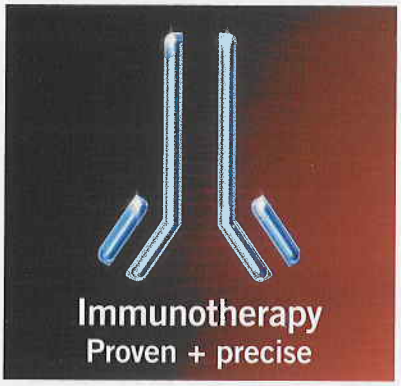
29% Patients failed to achieve a CR/CRu after two years of R-maintenance

26% Patients progressed with a median follow-up of 36 months

When first-line treatment falls short, consider ZEVALIN.

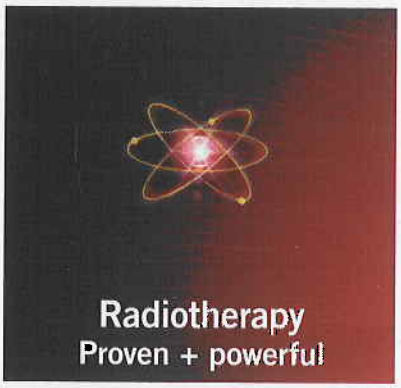
§ Note: Percentages are based on data provided in Salles 2010.[8]

ZEVALIN integrates two effective therapeutic approaches

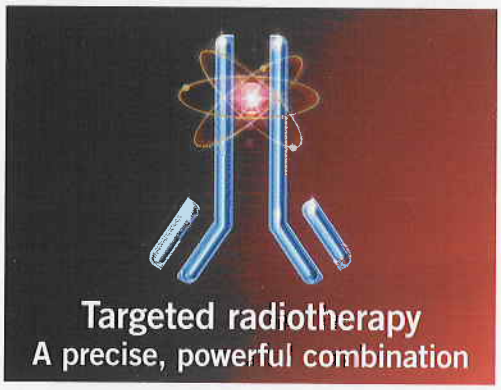


Treatment with CD20-targeted monoclonal antibodies has improved outcomes for follicular lymphoma patients.[10]

+



Follicular lymphomas are highly radiosensitive and radiotherapy is considered standard treatment for patients with early-stage, localized disease.[11]

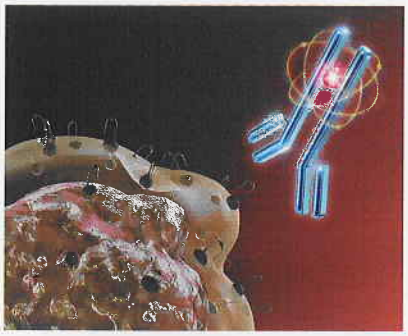


ZEVALIN pairs the precision of a monoclonal antibody with the power of radiotherapy in a single, chemo-free treatment.[12]

ZEVALIN is a pure beta emitter[13,14]

- Beta emissions have a shorter wavelength than gamma emissions, and require fewer precautions to minimize radiation exposure
- As a pure beta emitter, ZEVALIN can be administered in the outpatient setting—with minimal risk of radiation exposure to healthcare personnel, and no need to isolate patients after treatment
- Be sure to follow institutional good radiation safety practices and patient management procedures

ZEVALIN delivers radiation precisely where it's needed



Monoclonal antibody specifically targets the CD20 antigen found on 95% of B-cell lymphomas.[12,14]

Y-90 isotope attacks surrounding B-cells with high-energy beta radiation.[12,14]

Beta emission from Y-90 induces cellular damage through the formation of free radicals in the target and neighboring cells.[12,14]

Indications and Usage

ZEVALIN is a CD20-directed radiotherapeutic antibody administered as part of the ZEVALIN therapeutic regimen indicated for the treatment of patients with:

- Relapsed or refractory, low-grade or follicular B-cell non-Hodgkin's lymphoma (NHL)
- Previously untreated follicular NHL who achieve a partial or complete response to first-line chemotherapy

The maximum dose of Y-90 ZEVALIN is 32.0 mCi (1184 MBq).

Please see Important Safety Information on pages 2–3. Please see full Prescribing Information, including BOXED WARNINGS, for ZEVALIN included in the back pocket.

ZEVALIN®
ibritumomab tiuxetan
INJECTION FOR INTRAVENOUS USE

The **mAb** with **more**

In relapsed or refractory, low-grade or follicular B-cell NHL,

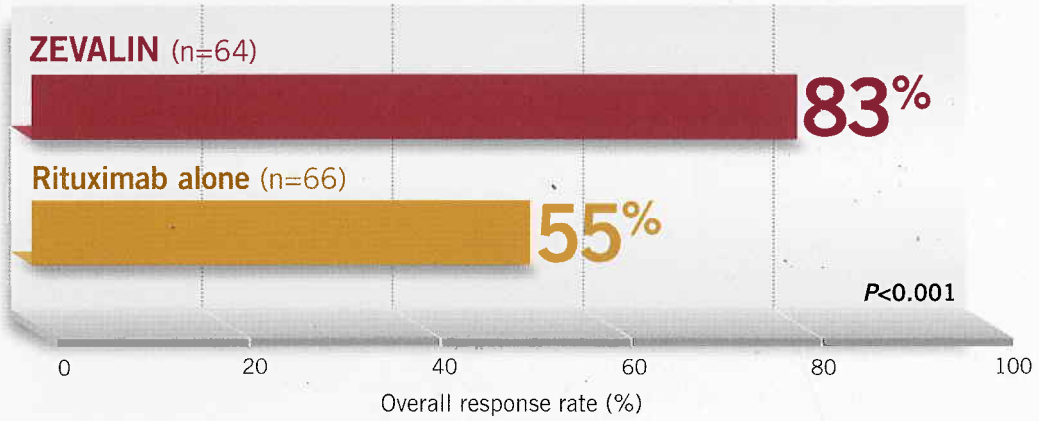
ZEVALIN treatment regimen delivers high response rates

Versus rituximab alone, ZEVALIN delivered higher response rates[12]

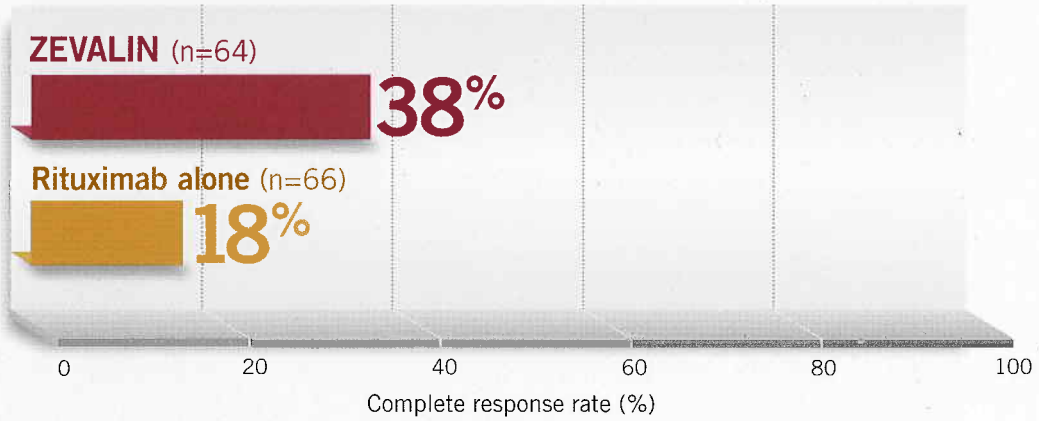
REGISTRATIONAL STUDY 2

Relapsed or refractory, low-grade or follicular NHL

Overall response rate (ORR)



Complete response rate



- ZEVALIN patients experienced a median time to progression of 12.1 months vs. 10.1 months for rituximab patients
- ZEVALIN patients experienced a median duration of response of 14.3 months vs. 11.5 months for rituximab patients

A randomized (1:1), open-label, multicenter study of 130 patients compared the ZEVALIN therapeutic regimen to rituximab given 375 mg/m^2 IV weekly for four doses. The primary endpoint of the study was ORR.

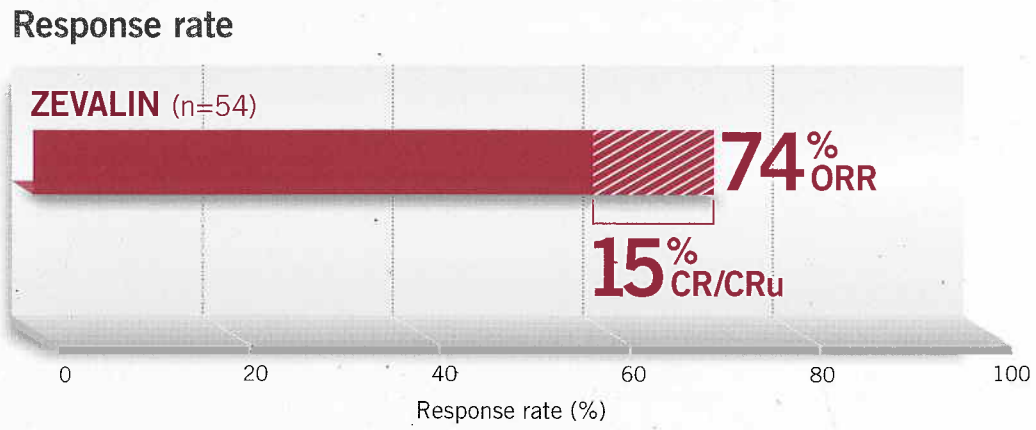
ZEVALIN treatment eligibility for patients with relapsed or refractory NHL

- Platelet counts ≥100,000/mm^3
- <25% bone marrow involvement

In relapsed patients *refractory to rituximab,* ZEVALIN delivered high response rates[12]

REGISTRATIONAL STUDY 1

Relapsed follicular lymphoma (refractory to rituximab treatment)



- ZEVALIN patients experienced a median time to progression of 6.8 months
- ZEVALIN patients experienced a median duration of response of 6.4 months

ZEVALIN treatment was evaluated in a single-arm study of 54 patients with relapsed follicular lymphoma, who were refractory to rituximab treatment. Rituximab refractory was defined as failure to achieve a PR or CR or TTP <6 months. The primary endpoint of this study was ORR.

Adverse Reactions

The most common adverse reactions of ZEVALIN are cytopenias, fatigue, abdominal pain, nausea, nasopharyngitis, asthenia, diarrhea, cough, and pyrexia. Common adverse reactions (≥40%) in clinical trials were: neutropenia, leukopenia, thrombocytopenia, anemia, infection, asthenia, musculoskeletal symptoms, and gastrointestinal symptoms. The most serious adverse reactions of ZEVALIN are prolonged and severe cytopenias (thrombocytopenia, anemia, lymphopenia, neutropenia) and secondary malignancies.

ZEVALIN is classified NCCN® Category 1 in second-line and subsequent therapy for patients with follicular lymphoma.[15]

Please see Important Safety Information on pages 2–3. Please see full Prescribing Information, including BOXED WARNINGS, for ZEVALIN included in the back pocket.

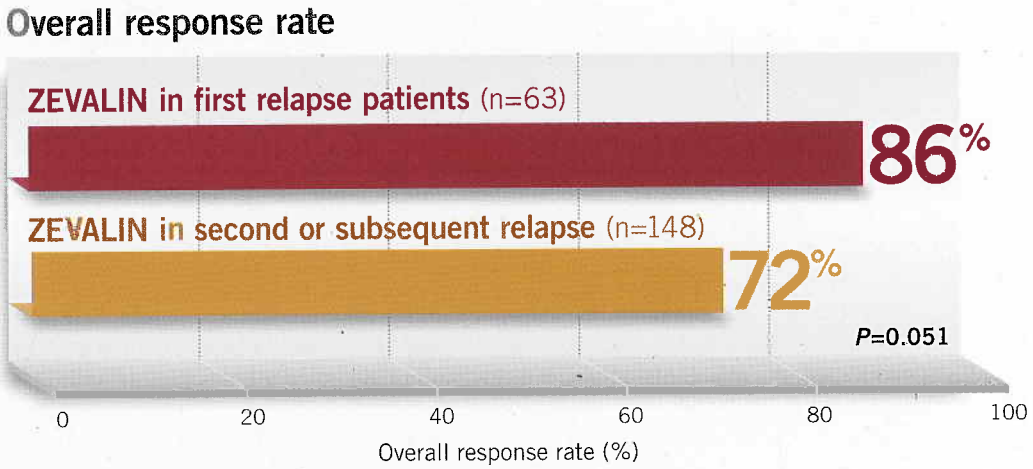
ZEVALIN®
ibritumomab tiuxetan
INJECTION FOR INTRAVENOUS USE

The **mAb** with **more**

In one analysis,

Earlier treatment with ZEVALIN treatment regimen was shown to provide benefits

Earlier treatment with ZEVALIN may improve ORR[16]



In patients with ORR after first relapse, ZEVALIN may improve median time to progression (TTP)[16]

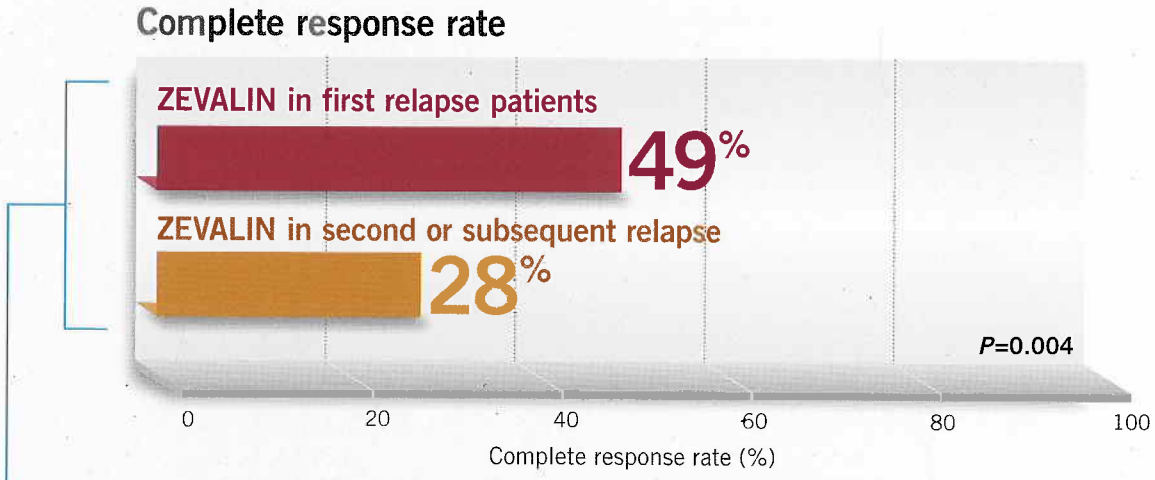
Median TTP was 12.6 months in patients at first relapse versus 7.9 months in patients at second or subsequent relapse (*P*=0.025).

Grade 3/4 Adverse Reactions

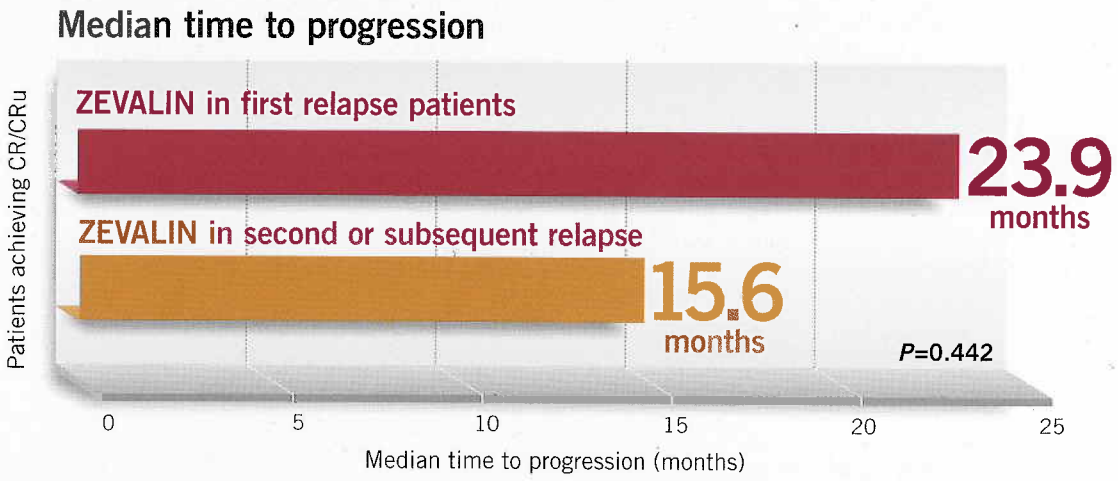
Grade 3/4 adverse reactions of ZEVALIN in relapsed or refractory NHL patients include prolonged and severe cytopenias (thrombocytopenia [63%], neutropenia [60%], anemia [17%], and ecchymosis [<1%]) and secondary malignancies. Serious infections occurred in 3% of patients (urinary tract infection, febrile neutropenia, sepsis, pneumonia, cellulitis, colitis, diarrhea, osteomyelitis, and upper respiratory tract infection). Life-threatening infections were reported in 2% of patients (sepsis, empyema, pneumonia, febrile neutropenia, fever, and biliary stent-associated cholangitis).

Please see Important Safety Information on pages 2–3. Please see full Prescribing Information, including BOXED WARNINGS, for ZEVALIN included in the back pocket.

Earlier treatment with ZEVALIN nearly doubled CR/CRu rates[16]



In patients with a CR/CRu after first relapse, ZEVALIN may improve median time to progression[16]



ZEVALIN offers your patients a different option: a single, chemo-free treatment course.

ZEVALIN®
ibritumomab tiuxetan
INJECTION FOR INTRAVENOUS USE

The **mAb** with **more**

In the relapsed/refractory setting,

Overall hematologic and non-hematologic adverse reactions

Most serious adverse reactions to ZEVALIN treatment regimen[12]

Prolonged and severe cytopenias and secondary malignancies

- Grade 3/4 cytopenia incidence rates in 349 patients who received ZEVALIN:
  - » Thrombocytopenia (63%)
  - » Neutropenia (60%)
  - » Anemia (17%)
  - » Ecchymosis (<1%)
- Myelodysplastic syndrome (MDS) and/or acute myelogenous leukemia (AML) were reported in 5.2% (11/211) of patients enrolled in clinical studies and 1.5% (8/535) of patients included in the expanded-access trial, with median follow-up of 6.5 and 4.4 years, respectively

Most common non-hematological adverse reactions to ZEVALIN[12]

- Fatigue
- Abdominal Pain
- Nausea
- Nasopharyngitis
- Asthenia
- Diarrhea
- Cough
- Pyrexia

Infusion reactions and extravasation[12]

- Immediately discontinue rituximab and ZEVALIN infusions for severe infusion reactions
- Temporarily slow or interrupt rituximab infusion for less severe infusion reactions
- Monitor patients closely for evidence of extravasation occurrence during injection of ZEVALIN and restart in another limb

Severe cutaneous and mucocutaneous reactions[12]

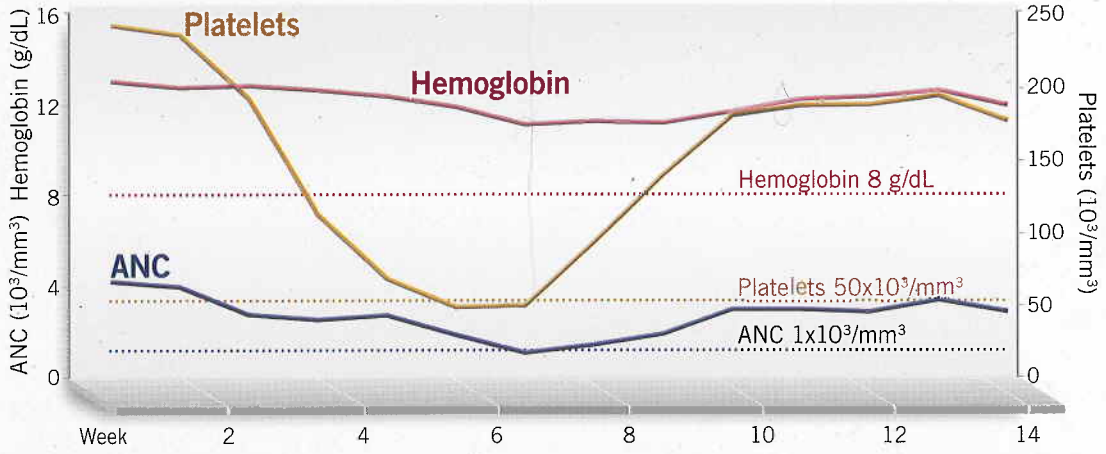
- Severe cutaneous and mucocutaneous reactions, some fatal, can occur with the ZEVALIN treatment regimen
- Discontinue rituximab and ZEVALIN infusions in patients experiencing severe cutaneous or mucocutaneous reactions

Serious infection occurred in 3% of patients[12]

- Included urinary tract infection, febrile neutropenia, sepsis, pneumonia, cellulitis, colitis, diarrhea, osteomyelitis, and upper respiratory tract infection
- Life-threatening infections reported in 2% of patients included sepsis, empyema, pneumonia, febrile neutropenia, fever, and biliary stent-associated cholangitis

Grade 3/4 hematological side effects in relapsed or refractory patients can be predictable and manageable*

Anticipated timelines for prolonged and severe cytopenias[12]



ANC=absolute neutrophil count

----- **Grade 3 toxicity levels**

Line graph adapted with permission from Witzig TE et al. *J Clin Oncol.* 2002;20(10):2459.[17]

*** Severe cytopenias persisting more than 12 weeks following administration can occur. Monitor patients for cytopenias and their complications (eg, febrile neutropenia, hemorrhage) for up to 3 months after use of the ZEVALIN therapeutic regimen.**

- Median recovery time from nadir to grade 1 toxicity or baseline is approximately 2 weeks for neutrophils and platelets
- Cytopenias more severe and prolonged among patients receiving ZEVALIN after first-line fludarabine or fludarabine-containing chemotherapy

Please see Important Safety Information on pages 2–3. Please see full Prescribing Information, including BOXED WARNINGS, for ZEVALIN included in the back pocket.

ZEVALIN®

ibritumomab tiuxetan

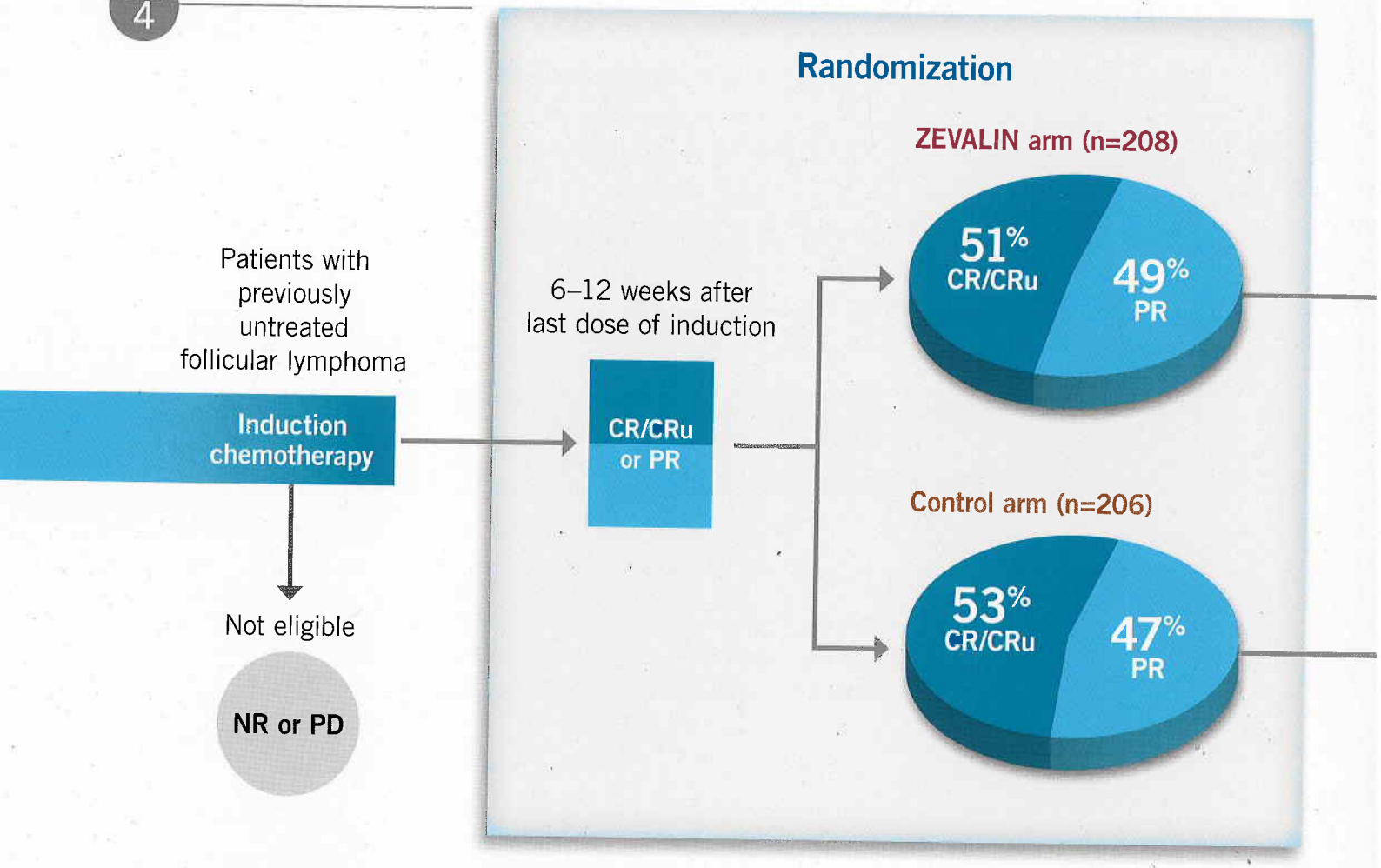
INJECTION FOR INTRAVENOUS USE

The **mAb** with **more**

In patients who responded to first-line induction chemotherapy,

ZEVALIN treatment regimen provides an effective next step

REGISTRATIONAL STUDY 4



ZEVALIN treatment eligibility for patients with previously untreated follicular NHL who achieve a PR or CR/CRu to first-line chemotherapy

- Platelet counts ≥150,000/mm^3
- <25% bone marrow involvement

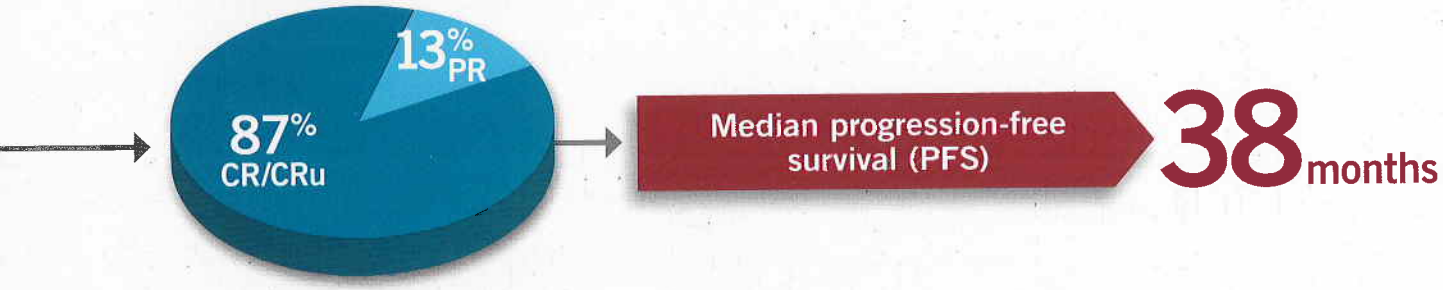
Patients with follicular lymphoma, who achieved a complete response (CR)/unconfirmed CR (CRu) or partial response (PR) after first-line induction chemotherapy, were assigned to receive either ZEVALIN or no further treatment. Randomization was stratified by center and response to first-line therapy (CR or PR). Baseline patient and disease characteristics were well-balanced between treatment arms.

NR = no response
PD = progressive disease

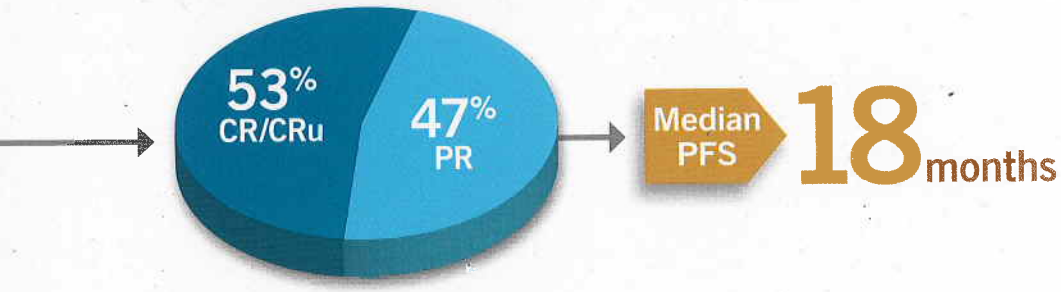
In patients who responded to first-line induction chemotherapy,

ZEVALIN consolidation more than doubles median PFS versus no further treatment

Post-consolidation with ZEVALIN[18,12]



No further treatment[18,12]



Please see Important Safety Information on pages 2–3. Please see full Prescribing Information, including BOXED WARNINGS, for ZEVALIN included in the back pocket.

Consolidation with ZEVALIN delivered median PFS of 38 months vs. 18 months with no further treatment (*P*<0.0001).[12]

ZEVALIN®
ibritumomab tiuxetan
INJECTION FOR INTRAVENOUS USE

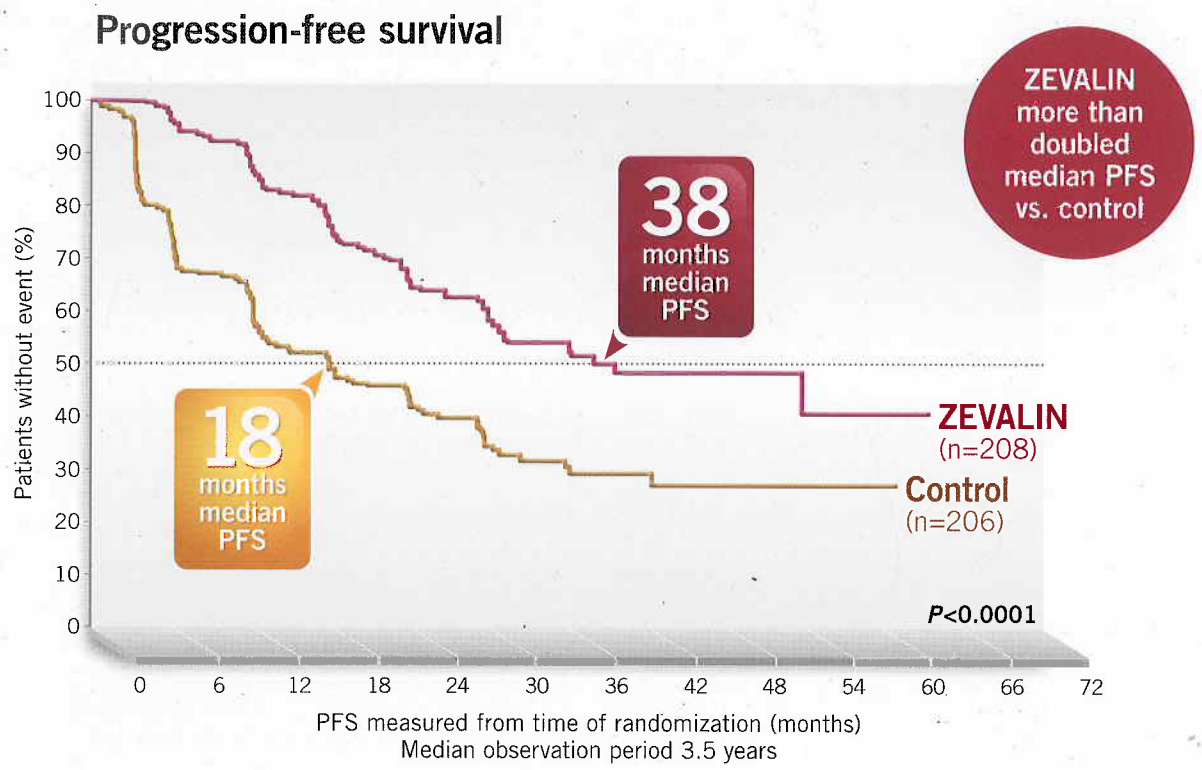
The **mAb** with **more**

After first-line induction chemotherapy,

ZEVALIN treatment regimen improves median PFS versus no further treatment

REGISTRATIONAL STUDY 4

At 3.5 year follow-up, ZEVALIN increased median PFS by 20 months versus no further treatment[12]



ZEVALIN treatment resulted in 54% risk reduction (HR=0.46 [95% CI: 0.35, 0.60]).

Please see Important Safety Information on pages 2–3. Please see full Prescribing Information, including BOXED WARNINGS, for ZEVALIN included in the back pocket.

In the registrational, multicenter, randomized, open-label study of 414 patients with follicular NHL, patients were randomized to receive ZEVALIN (n=208) or no further treatment (n=206).[12]

Induction chemotherapies received by patients in the study included:

- Single-agent chlorambucil (9.5%)
- Fludarabine or a fludarabine-containing regimen (5%)
- Cyclophosphamide-containing combination chemotherapy (71%) of which included CHOP (31%), CHOP-like (15%), and CVP/COP (26%)
- Rituximab-containing chemotherapy (14%)

Analysis of clinical study data showed no overall differences in ZEVALIN safety or efficacy in older patients

14% of patients who received ZEVALIN in the first-line setting were ≥65 years old.

Grade 3/4 Adverse Reactions

When administered following first-line chemotherapy, grade 3/4 adverse reactions of ZEVALIN include prolonged and severe cytopenias (thrombocytopenia [51%], neutropenia [41%], leukopenia [36%], lymphopenia [18%], and anemia [5%]) and secondary malignancies. Cytopenias were more severe and more prolonged among eleven (5%) patients who received ZEVALIN after first-line fludarabine or a fludarabine-containing chemotherapy regimen as compared to patients receiving non-fludarabine-containing regimens. Grade 3/4 infections occurred in 8% of ZEVALIN-treated patients and in 2% of controls and included neutropenic sepsis (1%), bronchitis, catheter sepsis, diverticulitis, herpes zoster, influenza, lower respiratory tract infection, sinusitis, and upper respiratory tract infection.

ZEVALIN is classified NCCN® Category 1 following first-line chemotherapy in patients with follicular lymphoma.[15]

ZEVALIN®
ibritumomab tiuxetan
INJECTION FOR INTRAVENOUS USE

The **mAb** with **more**

In first-line patients,

Overall hematologic and non-hematologic adverse reactions

Most serious adverse reactions to ZEVALIN treatment regimen[12]

Prolonged and severe cytopenias and secondary malignancies

- Grade 3/4 cytopenia incidence rates in 206 patients who received ZEVALIN:
  - » Thrombocytopenia (51%)
  - » Neutropenia (41%)
  - » Anemia (5%)
  - » Leukopenia (36%)
  - » Lymphopenia (18%)
- Two of 204 patients (1%) diagnosed with acute myelogenous leukemia (AML) approximately 2 and 3.3 years after receiving ZEVALIN following first-line chemotherapy, respectively

Most common non-hematological adverse reactions to ZEVALIN[12]

- Fatigue (33%)
- Nasopharyngitis (19%)
- Nausea (18%)
- Abdominal pain (17%)
- Asthenia (15%)
- Diarrhea (11%)
- Cough (11%)
- Pyrexia (10%)

Infusion reactions and extravasation[12]

- Immediately discontinue rituximab and ZEVALIN infusions for severe infusion reactions
- Temporarily slow or interrupt rituximab infusion for less severe infusion reactions
- Monitor patients closely for evidence of extravasation occurrence during injection of ZEVALIN and restart in another limb

Severe cutaneous and mucocutaneous reactions[12]

- Severe cutaneous and mucocutaneous reactions, some fatal, can occur with the ZEVALIN treatment regimen
- Discontinue rituximab and ZEVALIN infusions in patients experiencing severe cutaneous or mucocutaneous reactions

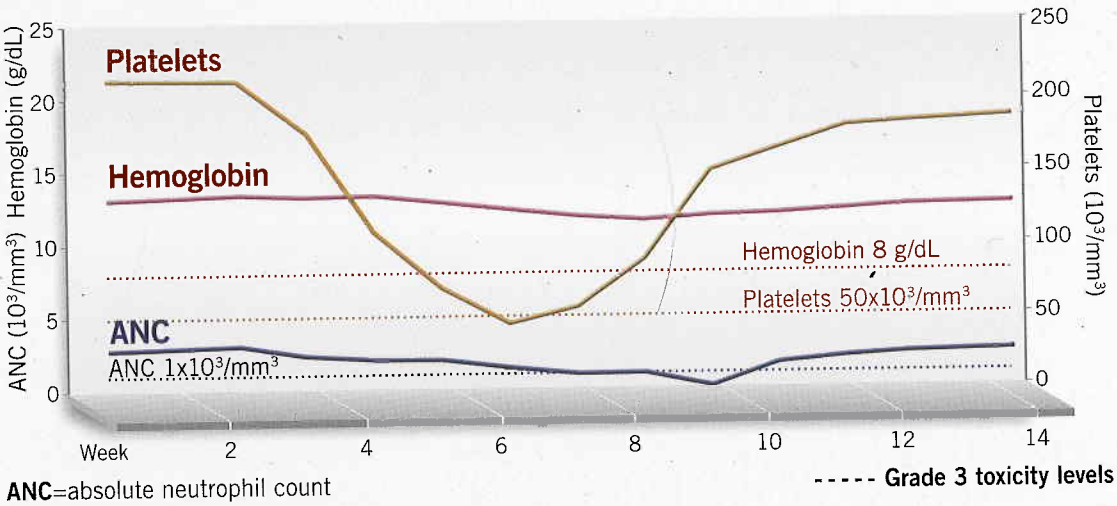
Grade 3/4 infections occurred in 8% of ZEVALIN-treated patients and in 2% of controls[12]

Included neutropenic sepsis (1%), bronchitis, catheter sepsis, diverticulitis, herpes zoster, influenza, upper and lower respiratory tract infection, and sinusitis.

Please see Important Safety Information on pages 2–3. Please see full Prescribing Information, including BOXED WARNINGS, for ZEVALIN included in the back pocket.

Grade 3/4 hematological side effects in patients following first-line induction chemotherapy can be predictable and manageable*

Anticipated timelines for prolonged and severe cytopenias[12]



Line graph adapted from Clinical Study Report (SAG 304820). Irvine, CA: Spectrum Pharmaceuticals, Inc; 2009.[19]

*** Severe cytopenias persisting more than 12 weeks following administration can occur. Monitor patients for cytopenias and their complications (eg, febrile neutropenia, hemorrhage) for up to 3 months after use of the ZEVALIN therapeutic regimen.**

- Median recovery time from nadir to grade 1 toxicity or baseline is approximately 2 weeks for neutrophils and platelets
- Cytopenias more severe and prolonged among patients receiving ZEVALIN after first-line fludarabine or fludarabine-containing chemotherapy

Updated Important Safety Information at 5.5 year follow-up[20]

- Secondary malignancies were observed in 16 patients in the ZEVALIN arm vs. 9 patients in the control arm (P=0.19)
- There were 6 cases of MDS/AML in the ZEVALIN arm vs. 1 case MDS in the control arm (P=0.063)†
- At 66 months median follow-up, 40 deaths of any cause have occurred: 18 in the ZEVALIN arm and 22 in the control arm (P=NS)

† The one case of MDS in the control arm received ZEVALIN off-protocol (Data on file: Spectrum Pharmaceuticals, Inc).

ZEVALIN®
ibritumomab tiuxetan
INJECTION FOR INTRAVENOUS USE

The **mAb** with **more**

ZEVALIN is delivered in a single treatment course

FDA removed Indium-111 bioscan 11/2011

RRZ: the ZEVALIN treatment regimen simplified[12]

- Premedicate with acetaminophen 650 mg and diphenhydramine 50 mg orally prior to rituximab infusion
- Intravenous injection of ZEVALIN over 10 minutes as follows:
  - » 0.4 mCi/kg (14.8 MBq per kg) for patients with normal platelet count
  - » 0.3 mCi/kg (11.1 MBq per kg) in relapsed or refractory patients with platelet count of ≥100,000 – ≤149,000 cells/mm^3
  - » The maximum dose of Y-90 ZEVALIN is 32.0 mCi (1184 MBq)
- Discontinue rituximab and ZEVALIN infusions in patients who develop severe infusion reactions or severe cutaneous or mucocutaneous reactions

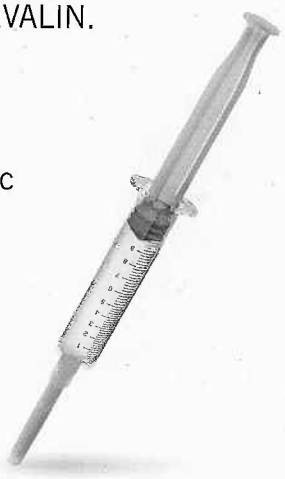
Straightforward for you and your patients

Our dedicated Clinical Logistics Specialists manage ZEVALIN treatment logistics

We're available to facilitate scheduling and pre- and post-treatment processes, helping ensure that every patient who is prescribed ZEVALIN gets ZEVALIN.

ZEVALIN is delivered as a patient-ready dose

A radiopharmacy will supply a unit dose of Y-90 ZEVALIN in a 10 cc pre-filled syringe, ready for patient administration.* Beyond the acrylic syringe shield, no additional protection is needed.



Patients receive the ZEVALIN injection in a single, 10-minute IV push—in the outpatient setting

ZEVALIN treatment uses beta-radiation, a form of radiation that requires only standard precautions to minimize radiation exposure. After ZEVALIN treatment, patients do not have to avoid contact with loved ones.

* Dose assay verification may be required based on local, state, and NRC regulation and licensing.

Your single source for reimbursement and patient access support:

Call *RESULTS*™

RESULTS™
Reimbursement Support Line-Trained Specialists

Before, during, and after treatment, *RESULTS*™ has your practice and your patients supported

For your practice.

Reimbursement simplified.

99% coverage by payers with no restrictions or prior authorization†

Use *RESULTS*™ to verify coverage and reimbursement in your area.

For your patients.

Access simplified.

Eligible patients get co-pay or insurance support‡

Use *RESULTS*™ to enroll patients to discover their options.

For every patient you consider for ZEVALIN:

Get *RESULTS*™
Call 866-298-8433

Monday–Friday 8:30 am–8:00 pm EST

† Coverage rate reflects experience when the *RESULTS*™ program is used. Based on 2011 *RESULTS*™ program reimbursement claims.[19]

‡ Patients with commercial insurance may be eligible for assistance with co-pays related with ZEVALIN therapy. Government insured patients (Medicare, Medicaid, etc) are not eligible for this program. Uninsured patients eligible for ZEVALIN treatment may be eligible for assistance.

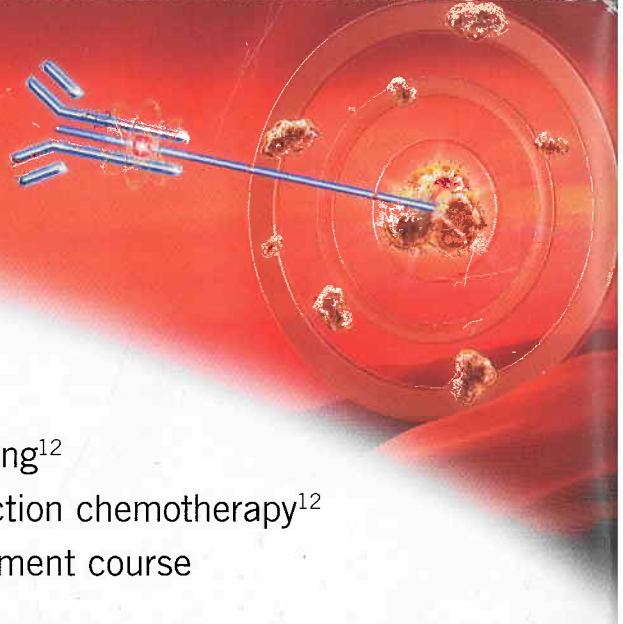
Please see Important Safety Information on pages 2–3. Please see full Prescribing Information, including BOXED WARNINGS, for ZEVALIN included in the back pocket.

ZEVALIN®
ibritumomab tiuxetan
INJECTION FOR INTRAVENOUS USE

The **mAb** with **more**

References

1. Friedberg JW, Taylor MD, Cerhan JR, et al. Follicular lymphoma in the United States: first report of the National LymphoCare Study. *J Clin Oncol.* 2009;27(8):1202-1208.
2. Flowers C, Taylor M, Hirata J, et al. Use of maintenance rituximab in the United States following R-based induction for follicular lymphoma [ASCO abstract 8100]. *J Clin Oncol.* 2010;28(15s)(suppl):abstr 8100.
3. Bachy E, Brice P, Delarue R, et al. Long-term follow-up of patients with newly diagnosed follicular lymphoma in the prerituximab era: effect of response quality on survival—a study from the Groupe d'Etude des Lymphomes de l'Adulte. *J Clin Oncol.* 2009;28(5):822-829.
4. Ghielmini M, Schmitz SF, Cogliatti SB, et al. Prolonged treatment with rituximab in patients with follicular lymphoma significantly increases event-free survival and response duration compared with the standard weekly × 4 schedule. *Blood.* 2004;103:4416-4423.
5. Czuczman AJ, Grillo-López CA, White M, et al. Treatment of patients with low-grade B-cell lymphoma with the combination of chimeric anti-CD20 monoclonal antibody and CHOP chemotherapy. *J Clin Oncol.* 1999;17(1): 268-276.
6. Hiddeman W, Kneba M, Dreyling M, et al. Frontline therapy with rituximab added to the combination of cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP) significantly improves the outcome for patients with advanced-stage follicular lymphoma compared with therapy with CHOP alone: results of a prospective randomized study of the German Low-Grade Lymphoma Study Group. *Blood.* 2005;106(12):3725-3732.
7. Marcus R, Imrie K, Belch A, et al. CVP chemotherapy plus rituximab compared with CVP as first-line treatment for advanced follicular lymphoma. *Blood.* 2005;105(4):1417-1423.
8. Salles G, Seymour JF, Offner F, et al. Rituximab maintenance for 2 years in patients with high tumour burden follicular lymphoma responding to rituximab plus chemotherapy (PRIMA): a phase 3, randomized controlled trial. *Lancet.* 2010;377:42-51.
9. Rummel MJ, Niederle N, Banat AG, et al. Bendamustine plus rituximab (B-R) versus CHOP plus rituximab (CHOP-R) as first-line treatment in patients with indolent and mantle cell lymphomas (MCL): Updated results from the StiL NHL1 study [ASCO abstract 3]. *J Clin Oncol.* 2012;30(suppl):abstr 3.
10. Efrat D, Aggarawal C, Smith MR. Impact of rituximab (rituxan) on the treatment of B-cell non-Hodgkin's lymphoma. *P&T.* 2010;35(3):148-157.
11. Pugh TJ, Ballonoff A, Newman F, Rabinovitch R. Improved survival in patients with early stage low-grade follicular lymphoma treated with radiation. *Cancer.* 2010;116(16):3843-3851.
12. ZEVALIN [package insert]. Irvine, CA: Spectrum Pharmaceuticals, Inc.
13. Zhu X. Radiation safety considerations with yttrium 90 ibritumomab tiuxetan (Zevalin). *Semin Nucl Med.* 2004;34(1) (suppl):20-23.
14. Witzig TE, White CA, Wiseman GA, et al. Phase I/II trial of IDEC-Y2B8 radioimmunotherapy for treatment of relapsed or refractory CD20+ B-cell non-Hodgkin's lymphoma. *J Clin Oncol.* 1999;17(12):3793-3803.
15. Referenced with permission from The NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Non-Hodgkin's Lymphoma V.1.2013. ©National Comprehensive Cancer Network, Inc 2013. All rights reserved. Accessed January 4, 2013. To view the most recent and complete version of the guideline, go online to www.nccn.org. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, NCCN GUIDELINES®, and all other NCCN Content are trademarks owned by the National Comprehensive Cancer Network, Inc.
16. Emmanouilides C, Witzig TE, Gordon L, et al. Treatment with yttrium 90 ibritumomab tiuxetan at early relapse is safe and effective in patients with previously treated B-cell non-Hodgkin's lymphoma. *Leuk Lymphoma.* 2006;47(4):629-636.
17. Witzig TE, Gordon LI, Cabanillas F, et al. Randomized controlled trial of yttrium-90-labeled ibritumomab tiuxetan radioimmunotherapy vs. rituximab immunotherapy for patients with relapsed or refractory low-grade, follicular, or transformed B-cell non-Hodgkin's lymphoma. *J Clin Oncol.* 2002;20(10):2453-2463.
18. Morschhauser F, Radford J, Van Hoof A, et al. Phase III trial of consolidation therapy with yttrium-90-ibritumomab tiuxetan compared with no additional therapy after first remission in advanced follicular lymphoma. *J Clin Oncol.* 2008;26(32):5156-5163.
19. Data on file. Irvine, CA: Spectrum Pharmaceuticals, Inc.
20. Illidge T, Morschhauser F. Radioimmunotherapy in follicular lymphoma. *Best Pract Res Cl Ha.* 2011;24(2):279-293.



ZEVALIN combines a monoclonal antibody with radiotherapy to:

- Deliver high response rates in relapsed/refractory setting[12]
- Provide an effective next step following first-line induction chemotherapy[12]
- Offer a different option to your patients: a single treatment course

NCCN® CATEGORY 1
following first-line treatment in patients with follicular lymphoma

NCCN® CATEGORY 1
in second-line and subsequent therapy in patients with follicular lymphoma

Indications and Usage

ZEVALIN® (ibritumomab tiuxetan) is a CD20-directed radiotherapeutic antibody administered as part of the ZEVALIN therapeutic regimen indicated for the treatment of patients with:

- Relapsed or refractory, low-grade or follicular B-cell non-Hodgkin's lymphoma (NHL)
- Previously untreated follicular NHL who achieve a partial or complete response to first-line chemotherapy

Important Safety Information

WARNING: SERIOUS INFUSION REACTIONS, PROLONGED AND SEVERE CYTOPENIAS, and SEVERE CUTANEOUS AND MUCOCUTANEOUS REACTIONS

See full Prescribing Information for complete boxed warning.

- Serious Infusion Reactions, some fatal, may occur within 24 hours of rituximab infusion.
- Prolonged and Severe Cytopenias occur in most patients.
- Severe Cutaneous and Mucocutaneous Reactions, some fatal, reported with ZEVALIN therapeutic regimen.
- Do not exceed 32 mCi (1184 MBq) of Y-90 ZEVALIN.

Please see Important Safety Information on pages 2–3. Please see full Prescribing Information, including BOXED WARNINGS, for ZEVALIN included in the back pocket. Because the ZEVALIN therapeutic regimen includes the use of rituximab, please also consult Prescribing Information for rituximab (www.rituxan.com).

ZEVALIN®
ibritumomab tiuxetan
INJECTION FOR INTRAVENOUS USE

The **mAb** with **more**

SPECTRUM PHARMACEUTICALS
Redefining Cancer Care

0103-058300

ZEVALIN.com